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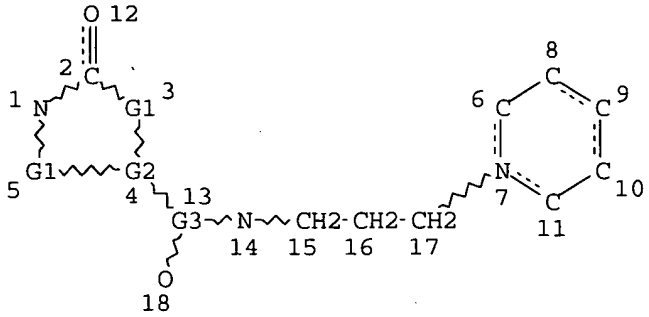
L1 STR



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VAR G3=C/S
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

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100.0% PROCESSED 13882 ITERATIONS 158 ANSWERS
SEARCH TIME: 00.00.01

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COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	163.48	163.69

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FILE COVERS 1907 - 3 May 2005 VOL 142 ISS 19
FILE LAST UPDATED: 2 May 2005 (20050502/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

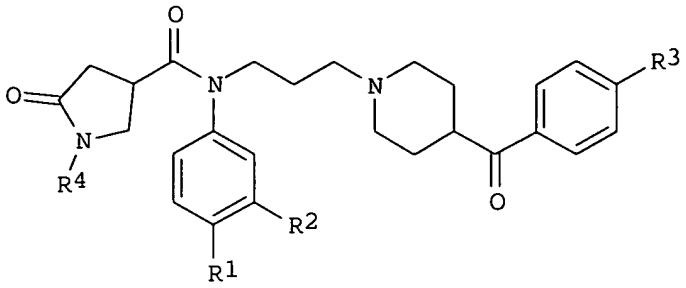
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 4 L3

=> d bib abs 1-4

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:306995 CAPLUS
DN 141:64392
TI CCR5 antagonists as anti-HIV-1 agents. Part 2: Synthesis and biological evaluation of N-[3-(4-benzylpiperidin-1-yl)propyl]-N,N'-diphenylureas
AU Imamura, Shinichi; Kurasawa, Osamu; Nara, Yoshi; Ichikawa, Takashi; Nishikawa, Youichi; Iida, Takehiro; Hashiguchi, Shohei; Kanzaki, Naoyuki; Iizawa, Yuji; Baba, Masanori; Sugihara, Yoshihiro
CS Pharmaceutical Research Division, Takeda Chemical Industries, Ltd., Osaka, Yodogawa-ku, 532-8686, Japan
SO Bioorganic & Medicinal Chemistry (2004), 12(9), 2295-2306
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 141:64392
AB The authors have previously reported the novel lead compound 1a as a CCR5 antagonist for treatment of HIV-1 infection. SAR studies on incorporating various acyl groups as a replacement for the 5-oxopyrrolidine-3-carbonyl group of the lead structure resulted in the discovery of N-[3-(4-benzylpiperidin-1-yl)propyl]-N,N'-diphenylurea with significantly improved CCR5 binding affinity. Substitutions (4-Cl and 4-Me) on the N'-Ph ring further increased the binding affinity. Introduction of polar substituents on the Ph ring of the 4-benzylpiperidine moiety enhanced the inhibitory activity of the HIV-1 envelope-mediated membrane fusion, suggesting that polar substituents at this position can interfere effectively with HIV-1 cell entry.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:144178 CAPLUS
DN 140:321219
TI CCR5 antagonists as anti-HIV-1 agents. 1. Synthesis and biological evaluation of 5-oxopyrrolidine-3-carboxamide derivatives
AU Imamura, Shinichi; Ishihara, Yuji; Hattori, Taeko; Kurasawa, Osamu; Matsushita, Yoshihiro; Sugihara, Yoshihiro; Kanzaki, Naoyuki; Iizawa, Yuji; Baba, Masanori; Hashiguchi, Shohei
CS Pharmaceutical Research Division, Takeda Chemical Industries, Ltd., Osaka, 532-8686, Japan
SO Chemical & Pharmaceutical Bulletin (2004), 52(1), 63-73
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English
GI



I

AB A novel lead compound, N-{3-[4-(4-fluorobenzoyl)piperidin-1-yl]propyl}-1-methyl-5-oxo-N-phenylpyrrolidine-3-carboxamide (I, R1, R2 = H, R3 = F, R4 = Me), was identified as a CCR5 antagonist by high-throughput screening using [125I]RANTES and CCR5-expressing CHO cells. The IC50 value of I was 1.9 μM. In an effort to improve the binding affinity of I, a series of 5-oxopyrrolidine-3-carboxamides was synthesized. Introduction of 3,4-dichloro substituents to the central Ph ring (I, R1, R2 = Cl, R3 = H, R4 = Me, IC50=0.057 μM; I, R1, R2 = Cl, R3 = F, R4 = Me, IC50=0.050 μM) or replacing the 1-Me group of the 5-oxopyrrolidine moiety with a 1-benzyl group (I, R1, R2, R3 = H, R4 = Bn, IC50=0.038 μM) was found to be effective for improving CCR5 affinity. The aforementioned compds. also inhibited CCR5-using HIV-1 envelope-mediated membrane fusion with IC50 values of 0.44, 0.19, and 0.49 μM, resp.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:855827 CAPLUS
DN 139:341780
TI Preventives for HIV infection containing CC chemokine receptor antagonists
IN Takashima, Katsunori; Iizawa, Yuji; Shiraishi, Mitsuru; Sugihara, Yoshihiro; Baba, Masanori
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 188 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

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PI	WO 2003089004	A1	20031030	WO 2003-JP4908	20030417
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	JP 2004043432	A2	20040212	JP 2003-113347	20030417
	EP 1498138	A1	20050119	EP 2003-719122	20030417
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	JP 2002-118055	A	20020419		
	JP 2002-141657	A	20020516		
	WO 2003-JP4908	W	20030417		

AB It is intended to provide a novel drug which exhibits an excellent effect

of preventing HIV infection in transfusing blood and using a blood preparation This object can be achieved by a preventive for HIV infection in transfusing blood and using a blood preparation characterized by containing a compound having antagonism to a CC chemokine receptor (preferably antagonism to CCR5 and/or CCR2). The anti-HIV infection effect of N,N-dimethyl-N-[4-[[[2-(4-methylphenyl)-6,7-dihydro-5H-benzocycloheptene-8-yl]carbonyl]amino]benzyl]-N-(4-tetrahydropyranyl)ammonium chloride (I) was examined in MOLT-4/CCR5 cells. A capsule containing I 40, lactose 70, fine crystalline cellulose 9, and magnesium stearate 1 mg was formulated.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:790471 CAPLUS
DN 133:350145
TI Preparation of cyclic amide compounds as chemokine receptor antagonists
IN Ishihara, Yuji; Imamura, Shinichi; Hashiguchi, Shohei; Nishimura, Osamu; Kanzaki, Naoyuki; Baba, Masanori
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000066551	A1	20001109	WO 2000-JP2765	20000427
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	JP 2001011073	A2	20010116	JP 2000-132861	20000427
	EP 1180513	A1	20020220	EP 2000-921055	20000427
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
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OS MARPAT 133:350145
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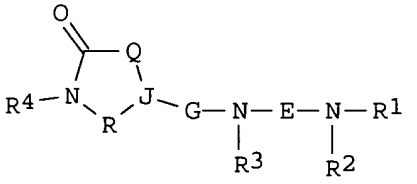

I

AB The title compds. I [R1 is hydrocarbyl and R2 is hydrocarbyl having two or more carbon atoms, or R1 and R2 together with the nitrogen atom adjacent thereto may form a ring which may be substituted; R3 is optionally substituted hydrocarbyl or a heterocyclic group; R4 is hydrogen, hydrocarbyl, a heterocyclic group, or the like; E is a divalent chain hydrocarbon group or the like; G is CO or SO2; J is nitrogen, a methine group, or the like; and Q and R are each a divalent C1-C3 chain hydrocarbon group or the like] are prepared I exhibit excellent CCR5

antagonism and are useful as preventive or therapeutic drugs for HIV infection of human peripheral blood monocytes, particularly AIDS. In an vitro test for CCR5 antagonism, N-[3-(4-benzyl-1-piperidinyl)propyl]-1-methyl-5-oxo-N-phenyl-3-pyrrolidinecarboxamide hydrochloride at 1 μM gave 57% inhibition of binding of RANTES to the CCR5 receptors. Formulations are given.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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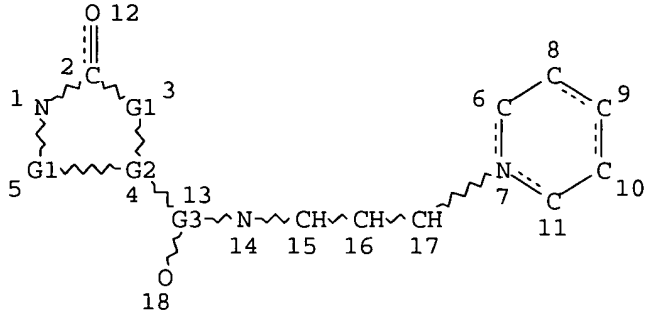


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  18

STEREO ATTRIBUTES: NONE


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                        BATCH   **COMPLETE**
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PROJECTED ANSWERS:               5 TO      234

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=> s l5 ful
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SEARCH TIME: 00.00.01

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L8             1 L7 NOT L3

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FILE COVERS 1907 - 3 May 2005  VOL 142 ISS 19
FILE LAST UPDATED: 2 May 2005  (20050502/ED)

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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

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L9            1 L8

=> d bib abs hitstr

L9   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2000:790471  CAPLUS
DN   133:350145
TI   Preparation of cyclic amide compounds as chemokine receptor antagonists
IN   Ishihara, Yuji; Imamura, Shinichi; Hashiguchi, Shohei; Nishimura, Osamu;
     Kanzaki, Naoyuki; Baba, Masanori
PA   Takeda Chemical Industries, Ltd., Japan
SO   PCT Int. Appl., 109 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
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             LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG,
             SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG,
             KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2371618            AA    20001109    CA 2000-2371618          20000427
     JP 2001011073         A2    20010116    JP 2000-132861           20000427
     EP 1180513            A1    20020220    EP 2000-921055           20000427
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
PRAI JP 1999-122549        A     19990428
     WO 2000-JP2765        W     20000427
OS   MARPAT 133:350145
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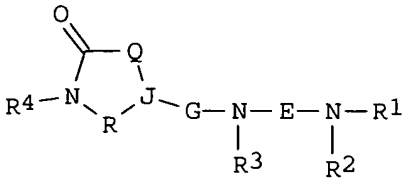


I

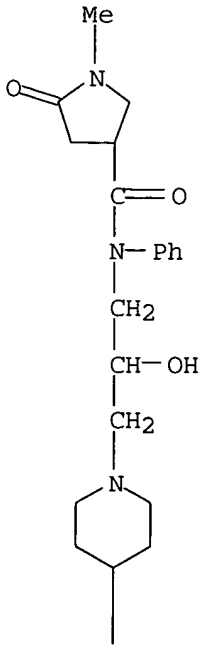
AB The title compds. I [R1 is hydrocarbyl and R2 is hydrocarbyl having two or more carbon atoms, or R1 and R2 together with the nitrogen atom adjacent thereto may form a ring which may be substituted; R3 is optionally substituted hydrocarbyl or a heterocyclic group; R4 is hydrogen, hydrocarbyl, a heterocyclic group, or the like; E is a divalent chain hydrocarbon group or the like; G is CO or SO2; J is nitrogen, a methine group, or the like; and Q and R are each a divalent C1-C3 chain hydrocarbon group or the like] are prepared I exhibit excellent CCR5 antagonism and are useful as preventive or therapeutic drugs for HIV infection of human peripheral blood monocytes, particularly AIDS. In an vitro test for CCR5 antagonism, N-[3-(4-benzyl-1-piperidinyl)propyl]-1-methyl-5-oxo-N-phenyl-3-pyrrolidinecarboxamide hydrochloride at 1 μM gave 57% inhibition of binding of RANTES to the CCR5 receptors. Formulations are given.

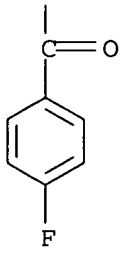
IT **304857-79-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic amide compds. as chemokine receptor antagonists)

RN 304857-79-2 CAPLUS

CN 3-Pyrrolidinecarboxamide, N-[3-[4-(4-fluorobenzoyl)-1-piperidinyl]-2-hydroxypropyl]-1-methyl-5-oxo-N-phenyl- (9CI) (CA INDEX NAME)

PAGE 1-A





RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT